

- 33 -

THAT WHICH IS CLAIMED IS:

1. An isolated nucleic acid active as an FSH β locus control region selected from the group consisting of:
 - (a) an isolated nucleic acid having the sequence given in SEQ ID NO:1 and encoding a sheep FSH β locus control region;
 - (b) an isolated nucleic acid at least 80% homologous to the isolated nucleic acid of (a) above and encoding an FSH β locus control region.
2. The isolated nucleic acid according to claim 1 selected from the group consisting of:
 - (a) an isolated nucleic acid having the sequence given in SEQ ID NO:1 and encoding a sheep FSH β locus control region;
 - (b) an isolated nucleic acid having the sequence given in SEQ ID NO: 3 and encoding a pig FSH β locus control region; and
 - (c) an isolated nucleic acid having the sequence given in SEQ ID NO: 5 and encoding a human FSH β locus control region.
3. The isolated nucleic acid according to claim 1 having the sequence given in SEQ ID NO:1 and encoding a sheep FSH β locus control region.
4. An isolated nucleic acid construct comprising at least one locus control region according to claim 1 operatively associated with a promoter.
5. The nucleic acid construct according to claim 4, wherein said promoter is a heterologous promoter.
6. The nucleic acid construct according to claim 4, wherein said promoter is a homologous promoter.
7. The nucleic acid construct according to claim 4, wherein said promoter is the FSH β promoter.

- 34 -

8. The nucleic acid construct according to claim 4, wherein said promoter is positioned 3' to said locus control region.

9. The nucleic acid construct according to claim 4, wherein said promoter is positioned 5' to said locus control region.

10. The nucleic acid construct according to claim 4, further comprising a nucleic acid of interest operatively associated with said promoter.

11. The nucleic acid construct according to claim 4, further comprising a nucleic acid encoding a protein or peptide operatively associated with said promoter.

12. The construct of claim 4, further comprising a nucleic acid encoding a tet receptor operatively associated with said promoter.

13. The construct of claim 4, wherein said nucleic acid is linear nucleic acid.

13. A vector comprising a nucleic acid construct according to claim 4.

14. The vector according to claim 12, wherein said vector comprises a plasmid containing said nucleic acid construct.

15. The vector according to claim 12, wherein said vector is a liposome carrying said nucleic acid.

16. A method of transforming a host cell, comprising:

- (a) providing a nucleic acid construct according to claim 4; and then
- (b) introducing said construct into said host cell.

17. The method according to claim 16, wherein said host cell is a mammalian cell.

- 35 -

18. The method according to claim 16, wherein said host cell is an oocyte.
19. The method according to claim 16, wherein said host cell is a gonadotrope cell.
20. The method according to claim 16, wherein said introducing step is carried out by lipofection or microinjection.
21. The method according to claim 16, wherein said construct further comprises a nucleic acid of interest operatively associated with said promoter, and said nucleic acid of interest is transcribed in said host cell.
22. The method according to claim 16, wherein said construct further comprises a nucleic acid encoding a protein or peptide operatively associated with said promoter, and said protein or peptide is expressed in said host cell.
23. The method according to claim 16, wherein said construct further comprises a nucleic acid encoding a tet receptor operatively associated with said promoter, and said tet receptor is expressed in said host cell.
24. A recombinant host cell containing a nucleic acid construct according to claim 4.
25. The host cell of claim 24, wherein said host cell is a mammalian host cell.
26. The host cell of claim 24, wherein said host cell is an oocyte.
27. The host cell of claim 24, wherein said host cell is a gonadotrope cell.
28. The host cell of claim 24, wherein said construct further comprises a nucleic acid encoding a tet receptor operatively associated with said promoter, and said tet receptor is expressed in said host cell.

29. The host cell of claim 24, wherein said host cell is a mammalian anterior pituitary cell, said construct further comprises a nucleic acid encoding a heterologous protein or peptide, and said heterologous protein or peptide is expressed in said anterior pituitary cell.

30. The host cell of claim 24, wherein said nucleic acid encodes luciferase.

31. A method of making a non-human transgenic animal, comprising the steps of:

(a) providing a nucleic acid construct according to claim 4, said construct further comprising a nucleic acid of interest operatively associated with said promoter;

(b) introducing said nucleic acid construct into a mammalian oocyte;

(c) implanting said oocyte in a pseudopregnant female host; and then

(d) raising said transgenic animal to viability from said oocyte in said host; said transgenic animal comprising anterior pituitary cells that contain and transcribe said nucleic acid of interest.

32. The method of claim 31, wherein said animal is a mouse and said host is a mouse.

33. The method of claim 31, wherein said introducing step is carried out by microinjection.

34. The method of claim 31, wherein said nucleic acid comprises linear nucleic acid.

35. A transgenic non-human animal,
said animal comprising anterior pituitary cells that contain a nucleic acid construct according to claim 4, said construct further comprising a nucleic acid of

- 37 -

interest operatively associated with said promoter, with said anterior pituitary cells transcribing said nucleic acid of interest.

36. The animal of claim 35, wherein said animal selected from the group consisting of mice, sheep, pigs and cows.

37. The animal of claim 35, wherein said nucleic acid encodes a protein or peptide, and said anterior pituitary cells express said protein or peptide.

38. The animal of claim 35, wherein said nucleic acid encodes a mutated tet receptor, and said anterior pituitary cells express said mutated tet receptor.

39. The animal of claim 35, wherein said nucleic acid encodes luciferase, and said anterior pituitary cells express said luciferase.

40. The animal of claim 35, wherein said anterior pituitary cells are gonadotrope cells.

41. A recombinant nucleic acid, comprising:

(a) a response element; and

(b) a nucleic acid encoding FSH β operatively associated with said response element.

42. The recombinant nucleic acid of claim 41, wherein said FSH β is selected from the group consisting of mouse, sheep, cow or pig FSH β .

43. The recombinant nucleic acid according to claim 41, further comprising:

(c) an FSH β promoter;

(d) an FSH β locus control region operatively associated with said FSH β promoter; and

- 38 -

(e) a nucleic acid encoding a ligand-controllable receptor operatively associated with said FSH β promoter, wherein said receptor binds to said response element in the presence of said ligand when expressed in a host cell.

44. The recombinant nucleic acid of claim 43, wherein:
said response element is a tet operator;
said ligand-controllable receptor is a tetracycline-controllable transactivator fusion protein; and
said ligand is tetracycline or an analog thereof.

45. The recombinant nucleic acid of claim 43, wherein:
said response element is a progesterone receptor response element;
said ligand-controllable receptor is a progesterone-controllable transactivator protein; and
said ligand is progesterone or an analog thereof.

46. The recombinant nucleic acid of claim 43, wherein:
said response element is an estrogen receptor response element;
said ligand-controllable receptor is an estrogen-controllable transactivator protein; and
said ligand is estrogen or an analog thereof.

47. A host cell containing the recombinant nucleic acid of claim 43.

48. A method of making a non-human transgenic animal, comprising the steps of:
(a) providing a recombinant nucleic acid according to claim 43;
(b) introducing said nucleic acid construct into a mammalian oocyte;
(c) implanting said oocyte in a pseudopregnant female host; and then
(d) raising said transgenic animal to viability from said oocyte in said host;
wherein said animal produces greater levels of FSH β and greater numbers of gametes when administered said ligand than when not administered said ligand.

- 39 -

49. The method according to claim 48, wherein said animal is selected from the group consisting of mice, sheep, cows and pigs.

50. The method of claim 48, wherein said animal is a mouse and said host is a mouse.

51. The method of claim 48, wherein said introducing step is carried out by microinjection.

52. The method of claim 48, wherein said nucleic acid comprises linear nucleic acid.

53. A transgenic non-human animal, said animal comprising cells that contain:

- (a) a response element;
- (b) a nucleic acid encoding FSH β operatively associated with said response element;
- (c) an FSH β promoter;
- (d) an FSH β locus control region operatively associated with said FSH β promoter; and
- (e) a nucleic acid encoding a ligand-controllable receptor operatively associated with said FSH β promoter, wherein said receptor binds to said response element in the presence of said ligand when expressed in a host cell;
and wherein said animal produces greater levels of FSH β and greater numbers of gametes when administered said ligand than when not administered said ligand.

54. The animal of claim 53, wherein said animal is selected from the group consisting of mice, pigs, cows and sheep mouse.

55. The animal of claim 53, wherein said animal is a mouse.

- 40 -

56. The animal of acid of claim 53, wherein:
said response element is a tet operator;
said ligand-controllable receptor is a tetracycline-controllable transactivator fusion protein; and
said ligand is tetracycline or an analog thereof.

57. A method of enhancing the production of gametes in a transgenic non-human animal, comprising the steps of:

(a) providing a transgenic non-human animal, said animal comprising cells that contain:

- (i) a response element;
- (ii) a nucleic acid encoding FSH β operatively associated with said response element;
- (iii) an FSH β promoter;
- (iv) an FSH β locus control region operatively associated with said FSH β promoter; and
- (v) a nucleic acid encoding a ligand-controllable receptor operatively associated with said FSH β promoter, wherein said receptor binds to said response element in the presence of said ligand when expressed in a host cell;

(b) administering said ligand to said animal in an amount effective to (i) stimulate the production of FSH β in said animal above that found in a corresponding untransformed animal; and (ii) stimulate the production of gametes in said animal to a level greater than that found in the corresponding untransformed animal.

58. The method of claim 57, wherein said animal is a male, and said gametes are sperm.

59. The method of claim 58, further comprising the step of harvesting said sperm from said animal.

60. The method of claim 57, wherein said animal is a female, and said gametes are oocytes.

61. The method of claim 60, further comprising the step of harvesting said oocytes from said animal.

62. The method of claim 60, wherein said administering step is followed by the step of:

(c) mating said animal to produce a litter of offspring therefrom, the size of said litter being greater than the size of a litter produced by the corresponding untransformed animal.

63. The method of claim 57, wherein said administering step is carried out by feeding said ligand to said animal.

64. The method of claim 57, wherein said animal is selected from the group consisting of mice, pigs, sheep and cows.

65. The method of claim 57, wherein said animal is a mouse.

66. The method of claim 57, wherein:
said response element is a tet operator;
said ligand-controllable receptor is a tetracycline-controllable transactivator fusion protein; and
said ligand is tetracycline or an analog thereof.

67. A method of detecting a transforming growth factor β in a sample, comprising the steps of:

(a) providing a pituitary gonadotrope host cell that contains a nucleic acid construct according to claim 4, wherein said promoter is operatively associated with a nucleic acid encoding a detectable protein or peptide;

(b) contacting a sample suspected of containing transforming growth factor β to said cell; and then

- 42 -

(c) detecting the production of said detectable protein or peptide by said cell, the production of said detectable protein or peptide indicating the presence of a transforming growth factor β in said sample.

68. The method of claim 67, wherein said transforming growth factor β is a bone morphogenetic protein.

69. The method according to claim 67, wherein said detectable protein or peptide is a luciferase.

70. The method according to claim 67, wherein said detecting step is followed by the step of (d) determining the amount of said transforming growth factor β in said sample.